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(54) Title: METHOD AND COMPOSITION FOR INHIBITING ANGIOGENESIS

(57) Abstract

A method of inhibiting angiogenesis and preparations for use therein are disclosed. The preparations comprise compounds thereof capable of inhibiting vascularization. The method and preparations are especially applicable to the treatment of solid tumors including skin cancers for controlling tumor neovascularization and thereby arresting tumor enlargement.

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CLAIMS

We claim:

1. A method of inhibiting angiogenesis in a human patient, comprising administering to the patient a vascularization inhibitor comprising a peptide capable of inhibiting vascularization.

2. The method of claim 1 in which the patient is being treated for an internal tumor, and said inhibitor before administration is admixed with a slow release agent and thereafter a portion of the mixture is implanted in or adjacent to the tumor.

3. The method of claim 2 in which the tumor being treated is a skin cancer and said inhibitor before administration is admixed with a topical vehicle and thereafter applied to the surface of the skin cancer.

4. In the treatment of human patients having growing solid tumors with associated neovascularization, the method of retarding tumors growth comprising administering to the site of the patient's tumor a vascularization inhibitor comprising a peptide

capable of inhibiting vascularization, said inhibitor being applied to the tumor in an amount effective for retarding its enlargement.

5. A therapeutic product for controlling angiogenesis, comprising implantable pellets composed essentially of a slow release agent in admixture with a vascularization inhibitor comprising a peptide thereof capable of inhibiting vascularization.

6. A therapeutic product for controlling angiogenesis, comprising a topical vehicle in admixture with a vascularization inhibitor comprising a peptide capable of inhibiting vascularization.

7. A therapeutic product for controlling angiogenesis, comprising a parenteral therapeutic vehicle containing a vascularization comprising a peptide capable of inhibiting vascularization.

8. The therapeutic preparations of claims 5, 6 and 7 in which said inhibitor contains a region capable of inhibiting angiogenesis as determined by the rat corneal assay.

9. A therapeutic preparation for controlling angiogenesis, comprising a therapeutic vehicle containing a vascularization inhibitor comprising a peptide capable of inhibiting vascularization.

10. A composition capable of inhibiting vascularization consisting essentially of amino acids selected from Sequence Id. No. 1.

11. A composition capable of inhibiting vascularization consisting essentially of amino acids selected from Sequence Id. No. 2.

12. The composition of claim 11 wherein said peptide ranges from amino acid numbers 1-15.

13. The composition of claim 11 wherein said peptide ranges from amino acids numbers 11-25.

14. A composition capable of inhibiting vascularization which consists essentially of peptides having the amino acid sequences:

X - Gly - Val - Gln - Tyr - Arg - X

(Sequence Id. No. 12) wherein X are amino acids which do not destroy or interfere with inhibition of vascularization.

15. A composition capable of inhibiting vascularization consisting essentially of amino acids selected from sequence Id. No. 3.

16. A composition capable of inhibiting vascularization consisting essentially of amino acids selected from sequence Id. No. 4.

17. A composition capable of inhibiting vascularization consisting essentially of amino acids selected from sequence Id. No. 5.

18. A composition capable of inhibiting vascularization consisting essentially of amino acids selected from Sequence Id. No. 6 wherein X are amino acids which do not destroy or interfere with inhibition of vascularization.

19. A composition capable of inhibiting vascularization consisting essentially of amino acids selected from Sequence Id. No. 7 wherein X are amino acids which do not destroy or interfere with inhibition of vascularization.

20. A composition capable of inhibiting vascularization consisting essentially of a peptide mimic off TSP-I gene.

21. A composition capable of inhibiting vascularization consisting essentially of a peptide mimic off TSP-II gene.

22. The composition of Claims 10-19 wherein said composition is linked to a chemical carrier.

A. CLASSIFICATION OF SUBJECT MATTER

IPC(5) :A61K 37/02; C07K 7/06, 7/08, 7/10, 13/00
US CL :514/8, 12, 13, 14, 16
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 514/8, 12, 13, 14, 16, 21; 530/324, 326, 327, 329, 380, 381, 395

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

A-Geneseq 9, PIR 34, Swiss-Prot 23
search terms: SEQ ID NOS 2, 3, 6, 7

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US, A, 4,585,754 (Meisner et al.) 29 April 1986, see the Abstract.	22
X Y	US, A, 4,898,732 (Fernandez) 06 February 1990, column 1, lines 45-59 and 64-68, column 2, lines 9-15 and 29-56.	20,21 1-8,22
X,E Y	US, A, 5,190,918 (Deutch et al.) 02 March 1993, column 6, lines 45-60, column 11, lines 8-14.	1,4,9,18,19 2,3,5-8,22
X,E	US, A, 5,192,744 (Bouck et al.) 09 March 1993, see entire document.	1-22

[X] Further documents are listed in the continuation of Box C. [ ] See patent family annex.

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C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X Y	N.P. Bouck et al., "Current Communications In Molecular Biology", published 1989 by Cold Spring Harbor Laboratory Press (NY), "Suppressor Control of an Inhibitor of Angiogenesis", pages 179-183, see entire document.	9-21 1-8,22
X Y	The Journal Of Cell Biology, Volume 112, No. 5, issued March 1991, C.A. Prater et al., "The Properdin-like Type I Repeats of Human Thrombospondin Contain a Cell Attachment Site", pages 1031-1040, see page 1037, Figure 8.	19 22
X	The Journal Of Biological Chemistry, Volume 265, No. 11, issued 15 April 1990, M.K. Wirtz et al., "In Vivo and in vitro Noncovalent Association of Excised α1(I) Amino-terminal Propeptides with Mutant pNα2(I) Collagen Chains in Native Mutant Collagen in a Case of Ehlers-Danlos Syndrome, Type VII", pages 6312-6317, see Figures 4 and 6.	15, 22